

Application No.: 09/506,079  
Attorney Docket No.: 49321-16  
First Applicant's Name: Gail M. Clinton  
Application Filing Date: February 16, 2000  
Office Action Dated: December 7, 2007  
Date of Response: June 9, 2008  
Examiner: Anne L. Holleran

IN THE CLAIMS:

Applicants, pursuant to revised 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently amended) An isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:14 and 19-28, and fragments thereof of about 50 to 79 contiguous residues in length, wherein the polypeptide binds to the extracellular domain (ECD) of HER-2 with an affinity binding constant of at least  $10^8 \text{ M}^{-1}$ , and wherein the polypeptide comprises: with respect to SEQ ID NO:14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO:19, the position 2 Ser; with respect to SEQ ID NO:20, the position 5 Pro; with respect to SEQ ID NO:21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO:22, the position 16 Gln; with respect to SEQ ID NO:23, the position 18 Leu; with respect to SEQ ID NO:24, the position 21 Asp, Ala~~Ala~~ or Val; with respect to SEQ ID NO:25, the position 36 Ile; with respect to SEQ ID NO:26, the position 54 Arg; with respect to SEQ ID NO:27, the position 64 Leu; or with respect to SEQ ID NO:28, both the position 6 Pro and the position 73 Asn.

2. (Previously presented) The isolated polypeptide of claim 1, wherein the isolated polypeptide is from about 69 to 79 contiguous residues in length.

3. (Previously presented) The isolated polypeptide of claim 1, wherein the isolated polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NOS:14 and 19-28.

4-7. (Cancelled)

8. (Currently amended) An isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:15 and 29-38, and fragments thereof of about 80 to 419 contiguous residues in length, wherein the C-terminal 79 contiguous amino acids are present, wherein at least one N-linked glycosylation site is present, wherein the polypeptide binds to the

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extracellular domain (ECD) of HER-2 with an affinity binding constant of at least  $10^8 \text{ M}^{-1}$ , and wherein the polypeptide comprises: with respect to SEQ ID NO:15, at least one of the position 346 Pro and the position 413 Asp; with respect to SEQ ID NO:29, the position 342 Ser; with respect to SEQ ID NO:30, the position 345 Pro; with respect to SEQ ID NO:31, both the position 346 Leu and the position 413 Asp; with respect to SEQ ID NO:32, the position 356 Gln; with respect to SEQ ID NO:33, the position 358 Leu; with respect to SEQ ID NO:34, the position 361 Asp, Ala~~Ala~~ or Val; with respect to SEQ ID NO:35, the position 376 Ile; with respect to SEQ ID NO:36, the position 394 Arg; with respect to SEQ ID NO:37, the position 404 Leu; or with respect to SEQ ID NO:38, both the position 346 Pro and the position 413[[73]] Asn.

9. (Previously presented) The isolated polypeptide of claim 8, wherein the isolated polypeptide is from about 350 to 419 contiguous residues in length and at least three N-linked glycosylation sites are present.

10. (Previously presented) The isolated polypeptide of claim 8, wherein the isolated polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NOS:15 and 29-38.

11-17. (Cancelled)

18. (Currently amended) A pharmaceutical composition for treating solid tumors that overexpress HER-2, comprising an agent selected from the group consisting of: (a) an isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:14 and 19-28, and fragments thereof of about 50 to 79 contiguous residues in length, wherein the polypeptide binds to the extracellular domain (ECD) of HER-2 with an affinity binding constant of at least  $10^8 \text{ M}^{-1}$ , and wherein the polypeptide comprises: with respect to SEQ ID NO:14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO:19, the position 2 Ser; with respect to SEQ ID NO:20, the position 5 Pro; with respect to SEQ ID NO:21, both the

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position 6 Leu and the position 73 Asp; with respect to SEQ ID NO:22, the position 16 Gln; with respect to SEQ ID NO:23, the position 18 Leu; with respect to SEQ ID NO:24, the position 21 Asp, Ala~~Ala~~ or Val; with respect to SEQ ID NO:25, the position 36 Ile; with respect to SEQ ID NO:26, the position 54 Arg; with respect to SEQ ID NO:27, the position 64 Leu; or with respect to SEQ ID NO:28, both the position 6 Pro and the position 73 Asn; (b) an isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:15 and 29-38, and fragments thereof of about 80 to 419 contiguous residues in length, wherein the C terminal 79 contiguous amino acids are present, wherein at least one N-linked glycosylation site is present, and wherein the polypeptide binds to the extracellular domain (ECD) of HER-2 with an affinity binding constant of at least  $10^8 \text{ M}^{-1}$ [[ ]], and wherein the polypeptide comprises: with respect to SEQ ID NO:15, at least one of the position 346 Pro and the position 413 Asp; with respect to SEQ ID NO:29, the position 342 Ser; with respect to SEQ ID NO:30, the position 345 Pro; with respect to SEQ ID NO:31, both the position 346 Leu and the position 413 Asp; with respect to SEQ ID NO:32, the position 356 Gln; with respect to SEQ ID NO:33, the position 358 Leu; with respect to SEQ ID NO:34, the position 361 Asp, Ala~~Ala~~ or Val; with respect to SEQ ID NO:35, the position 376 Ile; with respect to SEQ ID NO:36, the position 394 Arg; with respect to SEQ ID NO:37, the position 404 Leu; or with respect to SEQ ID NO:38, both the position 346 Pro and the position 413[[73]] Asn; (c) a monoclonal antibody that binds to the extracellular domain (ECD) of HER-2; and (d) combinations thereof, and a pharmaceutically acceptable carrier, with the proviso that where the composition comprises the monoclonal antibody it also comprises at least one of the agents of (a) or (b).

19. (Previously presented) The pharmaceutical composition of claim 18, wherein the agent is the isolated polypeptide comprising the amino acid sequence selected from the group

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consisting of SEQ ID NOS:14 and 19-28, and fragments thereof of about 50 to 79 contiguous residues in length.

20. (Previously presented) The pharmaceutical composition of claim 18, wherein the agent is the combination of the isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:14 and 19-28, and fragments thereof of about 50 to 79 contiguous residues in length, and the monoclonal antibody that binds to the extracellular domain (ECD) of HER-2.

21-37. (Cancelled)

38. (Currently amended) An isolated polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NOS:14 and 19-28, wherein the polypeptide comprises: with respect to SEQ ID NO:14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO:19, the position 2 Ser; with respect to SEQ ID NO:20, the position 5 Pro; with respect to SEQ ID NO:21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO:22, the position 16 Gln; with respect to SEQ ID NO:23, the position 18 Leu; with respect to SEQ ID NO:24, the position 21 Asp, Ala~~Ala~~ or Val; with respect to SEQ ID NO:25, the position 36 Ile; with respect to SEQ ID NO:26, the position 54 Arg; with respect to SEQ ID NO:27, the position 64 Leu; or with respect to SEQ ID NO:28, both the position 6 Pro and the position 73 Asn.

39. (Currently amended) An isolated polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NOS:15 and 29-38, wherein the polypeptide comprises: with respect to SEQ ID NO:15, at least one of the position 346 Pro and the position 413 Asp; with respect to SEQ ID NO:29, the position 342 Ser; with respect to SEQ ID NO:30, the position 345 Pro; with respect to SEQ ID NO:31, both the position 346 Leu and the position 413 Asp; with respect to SEQ ID NO:32, the position 356 Gln; with respect to SEQ ID NO:33, the

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position 358 Leu; with respect to SEQ ID NO:34, the position 361 Asp, ~~Ala~~ or Val; with respect to SEQ ID NO:35, the position 376 Ile; with respect to SEQ ID NO:36, the position 394 Arg; with respect to SEQ ID NO:37, the position 404 Leu; or with respect to SEQ ID NO:38, both the position 346 Pro and the position 413 Asn.

40. (Previously presented) The pharmaceutical composition of claim 18, wherein the agent is the isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:15 and 29-38, and fragments thereof of about 80 to 419 contiguous residues in length.

41. (Previously presented) The pharmaceutical composition of claim 18, wherein the agent is the combination of the isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:15 and 29-38, and fragments thereof of about 80 to 419 contiguous residues in length, and the monoclonal antibody that binds to the extracellular domain (ECD) of HER-2.

42. (Previously presented) An isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, and fragments thereof of about 50 to 79 contiguous residues in length, wherein the polypeptide binds to the extracellular domain (ECD) of HER-2 with an affinity binding constant of at least  $10^8 \text{ M}^{-1}$ , and wherein the polypeptide comprises at least one of the position 6 Pro and the position 73 Asp.

43. (Previously presented) The isolated polypeptide of claim 42, wherein the isolated polypeptide is from about 69 to 79 contiguous residues in length.

44. (Previously presented) The isolated polypeptide of claim 42, wherein the isolated polypeptide comprises the amino acid sequence of SEQ ID NO:14.

45. (Previously presented) An isolated polypeptide consisting of the amino acid sequence of SEQ ID NO:14.

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46. (Previously presented) An isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO:15, and fragments thereof of about 80 to 419 contiguous residues in length, wherein the C-terminal 79 contiguous amino acids are present, wherein at least one N-linked glycosylation site is present, wherein the polypeptide binds to the extracellular domain (ECD) of HER-2 with an affinity binding constant of at least  $10^8 \text{ M}^{-1}$ , and wherein the polypeptide comprises at least one of the position 346 Pro and the position 413 Asp.

47. (Previously presented) The isolated polypeptide of claim 46, wherein the isolated polypeptide is from about 350 to 419 contiguous residues in length and at least three N-linked glycosylation sites are present.

48. (Previously presented) The isolated polypeptide of claim 46, wherein the isolated polypeptide comprises the amino acid sequence of SEQ ID NO:15.

49. (Previously presented) An isolated polypeptide consisting of the amino acid sequence of SEQ ID NO:15.